UNITED STATES DISTRICT COURT
SOUTHERN DISTRICT OF OHIO
EASTERN DIVISION

SHARON SWANSON,
Individually and as parent
And natural guardian of
D.S. a minor,

Plaintiffs,

Case No. 2:14-cv-1052
CHIEF JUDGE EDMUND A. SARGUS, JR.
Magistrate Judge Elizabeth P. Deavers

v.

ABBOTT LABORATORIES,
***et al.*,**

Defendants.

OPINION AND ORDER

This is a product liability case under Ohio Law arising from Plaintiff Sharon Swanson's ingestion of the antiepileptic drug, Depakote, during her pregnancy with her son, D.S. (together, "Plaintiffs") brought against Abbott Laboratories and Abbvie Inc. (together, "Defendants" or "Abbott"). Before the Court are Defendants' Motion for Summary Judgment, (ECF No. 88) and Plaintiffs' Motion for Partial Summary Judgment. (ECF No. 76.) Both motions are contested. Several motions regarding the expert witnesses to be presented at trial are also pending. For the reasons that follow, Defendants' Motion for Summary Judgment is **GRANTED** (ECF No. 88) and Plaintiffs' Motion for Partial Summary Judgment is **DENIED**. (ECF No. 76.)

I. BACKGROUND

A. Factual Background

On June 23, 1994, Plaintiff Sharon Swanson, was hospitalized for severe mania and diagnosed with Bipolar Disorder. (Defs.' Ex. 1 at 1–2, ECF No. 99-1.) While hospitalized, Dr. Richard Alan Freeland, a psychiatrist, treated Ms. Swanson's Bipolar Disorder with Lithium. (*Id.* at 2.) She was discharged on July 1, 1994. (*Id.* at 1.) After discharge, however, Lithium

proved ineffective, resulting in readmission to the hospital on July 5, 1994. (Defs.' Ex. 2 at 2, ECF No. 99-2.) She remained hospitalized for another two weeks and was released on July 20, 1994. (*Id.* at 1.) During the July 1994 hospitalization, Dr. Freeland changed Ms. Swanson's medications, switching her from Lithium to Depakote. (Ex. 3, ECF No. 99-3.) Ms. Swanson's discharge summary notes that she responded well to treatment with Depakote. (Defs.' Ex. 2 at 1–2.)

Dr. Freeland testified that he was aware of teratogenic risks of Depakote and advised women in their childbearing years of the risks associated with Depakote and pregnancy, including advising patients to take birth control and avoid pregnancy while taking Depakote. (Freeland Dep. at 86:23–25; 87:1–25; 44:10–24; 45:10–18; 113:1–7, ECF No. 89-3.) In June 1995, Ms. Swanson went off of Depakote in order to conceive, which she did in December 1995. (*See* Defs.' Ex. 6 at 2, ECF No. 99-6 ("stopped taking meds 6/95 for desired pregnancy").) Ms. Swanson did not take Depakote at the time of conception nor through the first half of her pregnancy with D.S.

In April 1996, 20 weeks into her pregnancy, Ms. Swanson suffered another manic episode, resulting in hospitalization. (*Id.*) Aware of the teratogenic effects of Depakote, Dr. Freeland consulted with colleagues and Ms. Swanson's obstetrician as well as reviewing some of the available literature to weigh the risks of prescribing Depakote after the first trimester of a pregnancy. (Freeland Dep. 97:1–25; 98:1–10, ECF No. 89-3.) He ultimately prescribed Depakote, finding that she "had not tolerated lithium or responded especially well to it when used previously" but that she "appeared to respond well to Depakote previously [and] had been stable on Depakote." (Freeland Dep. 98:10–21, ECF No. 89-3.)

Plaintiff gave birth to D.S. in August of 1996 and D.S. was subsequently diagnosed with developmental delays including a diminished IQ and Autism Spectrum Disorder. (Defs.' Ex. 14 at 1–2, 6 ECF No. 99-11.) D.S. has also been diagnosed with a mood disorder. (*See id.* at 7.) Plaintiffs do not argue that the mood disorder is a result of Depakote exposure. Plaintiffs contend that D.S.'s autism and diminished capacity resulted from D.S.'s *in utero* exposure to

Depakote. (Pl.'s Resp. in Opp. at 2, ECF No. 127.) Plaintiff asserts that Defendants failed to adequately warn and instruct her and her prescribers of the degree and scope of Depakote's teratogenic risks during her pregnancy. (*Id.*)

Depakote was introduced into the United States market in 1983 for the treatment of seizures. It was later approved for the additional treatment of bipolar disorder and migraines. Depakote contains valproic acid, which is a teratogen.[1] It is undisputed that as of 1996 scientific evidence of teratogenic risks associated with exposure to Depakote during the first trimester of a pregnancy existed. (Defs.' Reply at 3, ECF No. 161.) Defendants, however, dispute that evidence of teratogenic risks from exposure to Depakote beginning after the second trimester existed during Swanson's pregnancy. (Defs.' Mot. Summ. J. at 7–9.) Rather, Defendants argue that in 1996, no scientific evidence supported a theory that *in utero* exposure to Depakote after the first trimester would increase the risk of developmental delays. (Defs.' Reply at 4, ECF No. 161 ("The American Academy of Neurology's 1992 consensus guidelines described Depakote's teratogenic risks as risks of this first trimester . . .").)

In 1996, Depakote's box warning stated:

> TERATOGENICITY:
> VALPROATE CAN PRODUCE TERATOGENIC EFFECTS SUCH AS NEURAL TUBE DEFECT (E.G. SPINA BIFIDA), ACCORDINGLY, THE USE OF DEPAKOTE TABLETS IN WOMEN OF CHILDBEARING POTENTIAL REQUIRES THAT THE BENEFITS OF ITS USE BE WEIGHED AGAINST THE RISK OF INJURY TO THE FETUS. THIS IS ESPECIALLY IMPORTANT WHEN THE TREATMENT OF A SPONTANEOUSLY REVERSIBLE CONDITION NOT ORDINARILY ASSOCIATED WITH PERMANENT INJURY OR RISK OF DEATH (E.G. MIGRANES) IS CONTEMPLATED, SEE WARNINGS, INFORMATION FOR PATIENTS. AN INFORMATION SHEET DESCRIBING THE TERATOGENIC POTENTIAL OF VALPROATE IS AVAILABLE FOR PATIENTS.

(Ex. 4, 1996 Package Insert at PAGEID #: 13287, ECF 118-4.)

[1] A teratogen is any agent that causes an abnormality following fetal exposure during pregnancy.

The 1996 label also included the following information in the "Usage and Pregnancy" Section of the label:

> **Usage in Pregnancy**
> ACCORDING TO PUBLISHED AND UNPUBLISHED REPORTS, VALPROIC ACID MAY PRODUCE TERATOGENIC EFFECTS IN THE OFFSPRING OF HUMAN FEMALES RECEIEVING THE DRUG DURING PREGNANCY.
>
> THERE ARE MULTIPLE REPORTS IN THE CLINICAL LITERATURE WHICH INDICATE THAT THE USE OF ANTIEPILEPTIC DRUGS DURING PREGNANCY RESULTS IN AN INCREASED INCIDENCE OF BIRTH DEFECTS IN THE OFFSPRING. ALTHOUGH DATA ARE MORE EXTENSIVE WITH RESPECT TO TRIMETHADIONE, PARAMETHADIONE, PHENYTOIN, AND PHENOBARBITAL, REPORTS INDICATE A POSSIBLE SIMILAR ASSOCIATION WITH THE USE OF OTHER ANTIEPILEPTIC DRUGS.
>
> THE INCIDENCE OF NEURAL TUBE DEFECTS IN THE FETUS MAY BE INCREASED IN MOTHERS RECEIVING VALPROATE DURING THE FIRST TRIMESTER OF PREGNANCY. THE CENTERS FOR DISEASE CONTROL (CDC) HAS ESTIMATED THE RISK OF VALPROIC ACID EXPOSED WOMEN HAVING CHILDREN WITH SPINA BIFIDA TO BE APPROXIMATELY 1 TO 2%.
>
> OTHER CONGENITAL ANOMALIES (E.G., CRANIOFACIAL DEFECTS, CARDIOVASCULAR MALFORMATIONS AND ANOMOLIES INVOLVING VARIOUS BODY SYSTEMS), COMPATIBLE AND INCOMPATIBLE WITH LIFE, HAVE BEEN REPORTED. SUFFICIENT DATA TO DETERMINE THE INCIDENCE OF THESE CONGENITAL ANOMALIES IS NOT AVAILABLE.
>
> THE HIGHER INCIDENCE OF CONGENITAL ANOMALIES IN ANTIEPILEPTIC DRUG-TREATED WOMEN WITH SEIZURE DISORDERS CANNOT BE REGARDED AS A CAUSE AND EFFECT RELATIONSHIP. THERE ARE INTRINSIC METHODOLOGIC PROBLEMS IN OBTAINING ADEQUATE DATA ON DRUG TERATOGENICITY IN HUMANS: GENETIC FACTORS OR THE EPILEPTIC CONDITION ITSELF, MAY BE MORE IMPORTANT THAN DRUG THERAPY IN CONSTRIBUTING TO CONGENITAL ANOMOLIES.

(*Id.* at PAGEID #: 13292.)

B. Procedural History

Plaintiffs filed this action on July 31, 2014. In the Complaint, Plaintiffs assert statutory claims of strict liability under theories of design defect, inadequate warning, and nonconformance with representations under common law negligence, negligent misrepresentation and fraud, breach of express warranty and implied warranties of merchantability, and unjust enrichment. Defendants raise multiple defenses including preemption.

On June 29, 2017, Plaintiffs filed a Partial Motion for Summary Judgment on Defendants' Preemption Defense (ECF No. 76) and Defendants filed a Motion for Summary Judgment on all claims. (ECF No. 88.) The parties have also filed several *Daubert* Motions seeking to exclude or limit expert testimony. Plaintiffs filed a Motion to Exclude the Expert Opinions of Dr. Max Wiznitzer and Dr. Deborah Leiderman. (ECF No. 84.) Defendants filed Motions to Exclude Certain Opinion Testimony of Dr. Joseph Piven (ECF No. 74), Florence Roullet (ECF No. 75), Dr. Michelle Riba (ECF No. 85), C. Ralph Buncher, SC.D. (ECF No. 86), and Dr. Suzanne Parisian. (ECF No. 87.) The Court defers ruling on the *Daubert* motions, unless necessary to the summary judgment order.

II. STANDARD OF REVIEW

Summary judgment is appropriate "if the movant shows that there is no genuine issue as to any material fact and the movant is entitled to judgment as a matter of law." Fed. R. Civ. P. 56(a). The Court may therefore grant a motion for summary judgment if the nonmoving party who has the burden of proof at trial fails to make a showing sufficient to establish the existence of an element that is essential to that party's case. *Celotex Corp. v. Catrett*, 477 U.S. 317, 322 (1986).

The "party seeking summary judgment always bears the initial responsibility of informing the district court of the basis for its motion, and identifying those portions" of the record which demonstrate "the absence of a genuine issue of material fact." *Celotex*, 477 U.S. at 323. The burden then shifts to the nonmoving party who "must set forth specific facts showing that there is a genuine issue for trial." *Anderson v. Liberty Lobby, Inc.*, 477 U.S. 242, 250 (1986) (quoting Fed. R. Civ. P. 56(e)). "The evidence of the nonmovant is to be believed, and all justifiable inferences are to be drawn in his favor." *Id.* at 255 (citing *Adickes v. S. H. Kress & Co.*, 398 U.S. 144, 158–59 (1970)). A genuine issue of material fact exists "if the evidence is such that a reasonable jury could return a verdict for the nonmoving party." *Id.* at 248; *see also Matsushita Elec. Indus. Co., Ltd. v. Zenith Radio Corp.*, 475 U.S. 574, 586 (1986) (The requirement that a dispute be "genuine" means that there must be more than "some metaphysical doubt as to the material facts."). Consequently, the central issue is "whether the evidence presents a sufficient disagreement to require submission to a jury or whether it is so one-sided that one party must prevail as a matter of law." *Hamad v. Woodcrest Condo. Ass'n*, 328 F.3d 224, 234–35 (6th Cir. 2003) (quoting *Anderson*, 477 U.S. at 251–52).

III. DISCUSSION

Defendants move for summary judgment on all claims, whereas Plaintiffs move for partial summary judgment on Defendants' preemption defense.

To begin with, the Court will consider the strict liability and negligent failure to warn claims. Defendants first contend that it cannot be liable for failing to warn of risks associated with the use of Depakote after the first trimester because no evidence or scientific literature in 1996 established that *in utero* Depakote exposure was associated with or could cause birth injuries in the absence of first trimester exposure. Defendants argue that as of 1996, the consensus within the medical community was that the medication's risk to the fetus was limited to exposure in the first trimester. In response, Plaintiffs argue that even without scientific

literature confirming, Abbott knew or should have known that the teratogenic effects of Depakote would continue beyond the first trimester because neurodevelopment continues beyond the first trimester. (Pls.' Resp. in Opp. at 16.) To the extent Plaintiffs' failure to warn claims are premised on a failure to warn about the risk of developmental delays resulting from *in utero* exposure, Defendants assert that such claims are preempted. Defendants also challenge Plaintiff's ability to prove causation and move for summary judgment on the remaining claims of design defect, negligent misrepresentation or fraud, breach of warranty, and unjust enrichment.[2]

A. Failure to Warn Claims

Plaintiffs allege Abbott's warning in 1996 was insufficient because it did not include warnings that risk from exposure to Depakote *in utero* extended beyond the first trimester, that the risk associated with use of Depakote is higher than with other medications, and that use increased the risk of causing developmental delays such as diminished IQ and Autism Spectrum Disorder. (Pls.' Resp. in Opp. at 9–11.)

1. Strict Liability and Negligence Standards for Failure to Warn

In Ohio, a plaintiff pursuing a product liability claim on a theory of failure to warn or failure to warn adequately may plead the allegations under both negligence and strict liability theories. *Cervelli v. Thompson/Center Arms*, 183 F. Supp. 2d 1032, 1040 (S.D. Ohio 2002) (citation omitted). Products liability claims in Ohio are government by the Ohio Products Liability Act ("OPLA"). O.R.C. § 2307.71 *et seq.* Under Ohio Revised Code § 2307.76, a product is defective due to inadequate warning or instruction if either of the following applies:

> (1) [A product] is defective due to inadequate warning or instruction at the time of marketing if, when it left the control of its manufacturer, both of the following applied:
> (a) The manufacturer knew or, in the exercise of reasonable care, should have

[2] Plaintiffs did not raise any argument in opposition to Defendants' Motion for Summary Judgment on the unjust enrichment claim and have thus waived their claim. *Humphrey v. U.S. Attorney Gen.'s Office*, 279 F. App'x 328, 331 (6th Cir. 2008) ("Thus where, as here, plaintiff has not raised arguments in the district court by virtue of his failure to oppose defendants' motions to dismiss, the arguments have been waived.") (citing *Resnick v. Patton*, 258 F. App'x 789, 793 n.1 (6th Cir. 2007)).

> known about a risk that is associated with the product and that allegedly caused harm for which the claimant seeks to recover compensatory damages;
> (b) The manufacturer failed to provide the warning or instruction that a manufacturer exercising reasonable care would have provided concerning that risk, in light of the likelihood that the product would cause harm of the type for which the claimant seeks to recover compensatory damages and in light of the likely seriousness of that harm.
>
> (B) A product is not defective due to lack of warning or instruction or inadequate warning or instruction as result of the failure of its manufacturer to warn or instruct about an open and obvious risk or a risk that is a matter of common knowledge.

"Under Ohio statutory law, a manufacturer is subject to liability for compensatory damages based on a product liability claim if the Plaintiffs prove, by a preponderance of the evidence, that the label was defective due to inadequate warning or instruction and the defect was the proximate cause of [plaintiff's] injury." *Rheinfrank v. Abbott Labs, Inc.*, 119 F. Supp. 3d 749, 760 (S.D. Ohio 2015). "A claim for negligent failure to warn has three basic elements: (1) a duty to warn against reasonably foreseeable risks; (2) breach of such duty; and (3) injury that is proximately caused by the breach." *Reece v. Astrazeneca Pharms., LP*, 500 F. Supp. 2d 736, 751 (S.D. Ohio 2007). "Because the standard for failure to warn requires that a manufacturer exercise reasonable care, the same standard applies for both strict liability and negligence claims for inadequate warning." *McConnell v. Costco, Inc.*, 238 F. Supp. 2d 970, 976 (S.D. Ohio 2003). Thus the Court will analyze the failure to warn claims together.

a. Preemption

Defendants assert that to the extent Plaintiffs claim Depakote's warnings were inadequate because they did not warn about a possible risk of cognitive delays, Plaintiffs' arguments are preempted. (Defs.' Mot. Summ. J. at 15.) Defendants contend that it was impossible for Abbott to have given any warning regarding developmental delay prior to 2011. Plaintiff similarly moved for summary judgment with respect to Defendants' preemption defense, asserting that Defendants do not meet their burden in proving impossibility. (Pls.' Mot. Summ. J. at 7, ECF

No. 76-2.)

Implied conflict preemption arises when "it is either impossible for a private party to comply with both state and federal requirements," *Rheinfrank*, 119 F. Supp. 3d at 762 (citing *Sprietsma v. Mercury Marine*, 537 U.S. 51, 64 (2002)), "or where state law stands as an obstacle to the accomplishment and execution of the full purposes and objectives of Congress." *Id.* (citation omitted). The Supreme Court of the United States explained in *Wyeth v. Levine*, that a failure to warn claim is preempted where the manufacturer of the drug can prove that it was impossible to comply with state and federal law with "clear evidence that the FDA would not have approved a change" to the drug's label. 555 U.S. 555, 571 (2009). As explained in *Rheinfrank*, the *Wyeth* Court did not define "clear evidence," but left the determination of what constitutes clear evidence to the lower courts. 119 F. Supp. 3d at 762. The Sixth Circuit affirmed *Rheinfrank's* finding of preemption, holding that the FDA's rejection of attempts to strength the drug label constituted clear evidence that the FDA would not have approved changes to the label. *Rheinfrank v. Abbott Labs., Inc.*, F. App'x 369, 385 (6th Cir. 2017) (affirming court's grant of summary judgment on Abbott's preemption defense for cognitive delay warnings "because the evidence in the record reveals that the FDA twice rejected Abbott's attempts to strengthen Depakote's label to add a developmental delay warning, there was clear enough evidence under *Wyeth* that the FDA would not have approved any such change in Depakote's label.").

The FDA regulates a manufacturer's marketing and labeling of its drugs. *See* 21 U.S.C. § 314.105(b). A manufacturer is required to submit a New Drug Application to the FDA demonstrating by substantial evidence that the medication is effacious prior to marketing it. *Rheinfrank*, 119 F. Supp. 3d at 762 (citing 21 U.S.C. § 314.105(b)). "The FDA's approval is then conditioned on the manufacturer's use of the label it suggests." *Id.* (citing *Mason v. SmithKline Beecham Corp.*, 596 F.3d 387, 391 (7th Cir. 2010)). To change labeling, the FDA provides:

The sponsor must submit a supplemental application fully explaining the basis for

> the change (§§ 314.70 and 601.12(f) (21 CFR 314.70 and 601.12(f))). FDA permits two kinds of labeling supplements: (1) Prior approval supplements, which require FDA approval before a change is made (§§ 314.70(b) and 601.12(f)(1); and (2) "changes being effected" (CBE) supplements, which may be implemented before FDA approval, but after FDA notification (§§ 314.70(c) and 601.12(f)(2)). While a sponsor is permitted to add risk information to the FPI without first obtaining FDA approval via a CBE supplement, FDA reviews all such submissions and may later deny approval of the supplement, and the labeling remains subject to enforcement action if the added information makes the labeling false or misleading under section 502(a) of the act (21 U.S.C. 352). Thus, in practice, manufacturers typically consult with FDA prior to adding risk information to labeling.

Requirements on Content and Format of Labeling for Human Prescription Drug and Biological Products, 71 Fed. Reg. 3922-01; *see also Rheinfrank*, 119 F. Supp. 3d at 762. The burden of proving an irreconcilable conflict exists is on the defendant. *Brown v. Earthboard Sports USA, Inc.*, 481 F.3d 901, 912 (6th Cir. 2007) ("[f]ederal preemption is an affirmative defense upon which the defendants bear the burden of proof."(internal quotations omitted)).

i. 2005–2006 Correspondence

In 2005, Abbott sought to add additional warning to the Depakote label through a Prior Approval Labeling Supplement ("PAS"). (Defs.' Ex. 18, ECF No. 88-18.) In the letter to Dr. Russell Katz, director of the division of Neuropharmacological Drug Products of the FDA, Abbott proposed to add new language to the label related to teratogenicity and developmental delay. Along with other modifications, the proposed language included, the additional warning: "THERE HAVE BEEN REPORTS OF DEVELOPMENTAL DELAY IN THE OFFSPRING OF WOMEN WHO HAVE RECEIVED VALPROIC ACID DURING PREGNANCY." (*Id.* at 5.)

Abbott attached a white paper to the correspondence entitled, "New information concerning the use of valproate in women of childbearing potential: teratogenicity and developmental delay," which discussed the scientific literature relevant to developmental delay in children exposed to Depakote and other anti-epileptic drugs ("AEDs") *in utero*. (*Id.* at 13–28.)

The FDA responded to the PAS through email on February 7, 2006, denying the use of

certain proposed language due to insufficient evidence. (Defs.' Ex. 19, ECF No. 88-19.) In the email the FDA wrote:

> The sentence "There have been reports of developmental delay in the offspring of women who have received valproic acid during pregnancy" is based on two recent publications (Gaily E et al. Neurology 62(1):28-32, 2004 and Vinten J et al. Neurology 64(6):949-54, 2005) that attempted to correlate children's performance on IQ assessments with maternal prenatal use of the valproate but which did not adequately control for maternal educational attainment. Maternal IQ and maternal educational attainment are known to strongly correlate with children's performance on IQ assessments and thus would confound any attempt to draw a correlation to maternal prenatal valproate use. Given the studies' inability to establish this correlation, the proposed sentence should not be incorporated into labeling. A similar proposed sentence in the Patient Information Leaflet was removed in the Approval Letter for S-032 (January 11, 2006).

(*Id.*)

ii. 2007–2008 Correspondence

In May 2007, Abbott wrote the FDA again to propose the inclusion of the language "There have been reports of developmental delay in the offspring of women who have received valproate during pregnancy." (Defs.' Ex. 20 at 3–4, ECF No. 88-20.) After reiterating the past communication, Abbott wrote that it had "continued to monitor the literature and our spontaneous adverse drug event (ADE) database for developmental delay associated with valproic acid. We provide an updated analysis of the occurrence of developmental delay in the attached white paper, which now includes more compelling data from the Neurodevelopment Effects of Antiepileptic Drugs (NEAD) study." (*Id.*) Abbott further requested that the FDA "provide advice on the acceptability of these data for use in revised labeling." (*Id.*)

In March 2008, after reviewing the submitted information and conducting its own literature review, the FDA again rejected Abbott's revision. (Defs.' Ex. 21, ECF No. 88-21.) The telephone conference record reflects that the FDA rejected the proposed language because "the data do not provide sufficient evidence to support [the] proposed labeling changes." (*Id.*)

iii. 2009 Correspondence

Abbott sent another letter to the FDA on April 30, 2009, requesting a labeling change for

developmental delay and/or autism/autism spectrum disorder after *in utero* exposure to Depakote. (Defs.' Ex. 22, ECF No. 88-22.) Once again Abbott provided the FDA with updated studies and attempted to convince the FDA that the labeling change was proper by pointing to "valproate labeling in other areas of the world" where developmental delay information had already been included. (*Id.* at 4.)

On September 18, 2009, Abbott representative held a teleconference with representatives from the FDA's Division of Neurology Products. (Defs.' Ex. 22, ECF No. 88-22.) The FDA rejected the proposed labeling changes, indicating that "the data available are not sufficiently compelling to be combined with Developmental Delay at this time." (*Id.*)

iv. 2011 Independent Review and Correspondence

In February 2011, the FDA wrote Abbott, explaining that it had undertaken an independent review of medical literature regarding an association between autism and Depakote exposure *in utero*. (Defs.' Ex. 16, ECF No. 88-16.) The FDA rejected the inclusion of language regarding autism and autism spectrum disorder on Depakote's labeling. The FDA wrote,

> Given the very small number of studies on the topic, as well as the confounding factors and the methodological limitations of the studies, the Division concluded that, although this issue should continue to be monitored, a causal relationship cannot be supported at this time. Therefore, the Division believes that it is inappropriate to include autism in the label other than in a listing of Post-Marketing adverse events reported.

(*Id.* at 3–4.)

Finally, in October 2011, the FDA agreed to the inclusion of a warning about the risk of developmental delay as proposed by Abbott. (Defs.' Ex. 24, ECF No. 88-24.)[3]

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[3] Plaintiffs argue against the admissibility of the email communications between Abbott and the FDA, contending that the communications are inadmissible hearsay. (Pls.' Resp. in Opp. at 40.) The Court, however, finds the communications admissible. A statement is only hearsay if "offer[ed] in evidence to prove the truth of the matter asserted in the statement." Fed. R. Evid. 801(c)(2). Defendants do not offer the communications as evidence that the inclusion of further warnings was inappropriate at the time period based on the discussed scientific offerings – but as evidence that the FDA rejected Abbott's attempt to include further warnings. *In re Nat'l Century. Fin. Enters.*, 846 F. Supp. 2d 828, 876 (S.D. Ohio 2012) ("If the significance of an offered statement lies solely in the fact that it was made, no issue is raised as to the truth of

v. Failure to Warn of Developmental Delay Claim is Preempted

Abbott asserts that it is entitled to judgment on Plaintiffs' failure to warn claims to the extent Plaintiffs claim Abbott failed to warn that *in utero* exposure to Depakote could increase risk of developmental delays, including autism. Abbott reasons that such claims are preempted by the FDA's multiple rejections of its attempt to include that warning. Plaintiffs also move for summary judgment on Abbott's preemption defense, arguing that Abbott cannot meet the high burden of proving impossibility because its First Amendment right to speak gave it the "means of complying with Ohio law and warning about Depakote's risks of developmental delay, autism, and/or autism spectrum disorder." (Pls.' Mot. Summ. J. at 7, ECF No. 76-1.)

As in *Rheinfrank*, preemption is warranted because there is clear evidence the FDA would not have approved a change to the Depakote label adding a developmental delay warning prior to D.S.'s injury. *See Rheinfrank*, 119 F. Supp. 3d at 766. In *Rheinfrank*, the district court found plaintiffs' failure to warn of developmental delay claims preempted based on the same facts discussed herein. The district court reasoned that any developmental claims were preempted,

> because there is clear evidence the FDA would not have approved a change to the Depakote label adding a developmental delay warning prior to M.B.D.'s injury. The Court finds the FDA's February 2006 decision that developmental delay warnings "should not be incorporated into [Depakote] labeling" and the FDA's 2008 belief that "the data do not provide sufficient evidence to support [Depakote] labeling changes at this time" constitute "clear evidence" that when confronted by the issue in 2003, the FDA would have rejected an attempt to add a developmental delay warning.

119 F. Supp. 3d at 766. The Sixth Circuit affirmed, finding the FDA's rejections of Abbott's

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anything asserted, and the statement is not hearsay.") (quoting Fed. R. Evid. 801, Advisory Committee Note to Subdivision (c), 1972 Proposed Rules)); *Peterson v. Kramer*, Case No. 3:13-cv-187, 2016 U.S. Dist. LEXIS 19938, at *20 (S.D. Ohio Feb. 17, 2016) (holding documents offered "to show that an investigation actually took place contrary to the [P]laintiff's allegations that no investigation took place" are not hearsay). The documents are relevant to establish the FDA's rejection of Abbott's attempts to enhance certain warnings, and are admissible in this action. *U.S. v. Boyd*, 640 F.3d 657, 664 (6th Cir. 2011) ("Statements to prove the listener's knowledge are not hearsay.").

attempts to strengthen its label constituted clear evidence that the FDA would not have approved any such change in Depakote's label under *Wyeth*. *Rheinfrank*, F. App'x at 385; *see also Z.H. v. Abbott Labs., Inc.*, 2016 U.S. Dist. LEXIS 135792, at *26 (N.D. Ohio Sept. 30, 2016) ("The courts in both *Rheinfrank* and *In re Depakote* rule in favor of Defendants . . . [f]inding that attempts by Depakote in 2006 and 2008 to amend its warning label to include warnings of developmental delay due to Depakote use were rejected by the FDA, the courts found Plaintiffs' claim for inadequate warnings of developmental delay were preempted by federal law."); *In re Depakote*, 87 F. Supp. 3d 916, 921–23 (S.D. Ill. 2015) (finding "clear evidence that the FDA would not have approved a developmental delay warning" before plaintiff's injury in 1999).

Plaintiffs argue that Defendants have not met their burden in proving impossibility because the First Amendment protects their right to communicate non-FDA approved information through other means, such as Dear Doctor letters. (Pls.' Mot. Summ. J. at 9–11.) In support, Plaintiffs cite cases holding that the First Amendment does not allow the FDA to prohibit truthful and non-misleading promotion of a drug for off label uses by its manufacturer. (*Id.* at 9–10.) Such cases, however, are not applicable in the instant matter. As Defendants correctly aver, the ability to promote off-label uses is irrelevant as to whether the FDA's rejection of a labeling change for an on-label use constitutes clear evidence of conflict with state law. (Defs.' Resp. in Opp. at 3, ECF No. 124.)

In fact, the FDA has control over prescription drug labeling under the Food Drug and Cosmetic Act. *See* 21 U.S.C. § 321 (m)–(n). Under the act, what is considered 'labeling' is construed broadly and includes the Dear Doctor letters Plaintiffs argue Abbott should have sent. *PLIVA, Inc. v. Mensing*, 564 U.S. 604, 623–24 (2011) ("A Dear Doctor letter that contained substantial new warning information would not be consistent with the drug's approved labeling. . . . Accordingly, we conclude that federal law did not permit the Manufacturers to issue additional warnings through Dear Doctor letters."); *Fulgenzi v. PLIVA, Inc.*, 711 F.3d 578, 581 n.1 (6th Cir. 2013) ("The FDA construes 'labeling' broadly, to include not just the written label associated with the drug, but communications with physicians and other healthcare professionals containing

additional warnings ('Dear Doctor' letters) and information published in the Physician's Desk Reference."). To hold that Defendants' First Amendment right prevents preemption is contrary to case law finding preemption based on FDA regulations. *PLIVA*, 564 U.S. at 623–24; *Mut. Pharm. Co. v. Bartlett*, 133 S. Ct. 2466, 2470 (2013) ("state-law design-defect claims that turn on the adequacy of a drug's warnings are pre-empted by federal law under PLIVA").

Plaintiffs also argue that Abbott errs in conflating autism and developmental delay, contending that Abbott and the FDA treated the conditions as distinct during the aforementioned communications. (Pls.' Resp. in Opp. at 39.) In argument that autism is a developmental delay, Abbott quotes Plaintiffs' expert Dr. Piven, who defined autism as a developmental delay. (Piven Dep. 37:8–14, ECF No. 89-2 (Q. "So, Doctor, are you saying that you put autism in the category of developmental disorders?" A. "Yes. I think everyone would." Q. "And you would put autism in the category of developmental delay?" A. "Yes.").) This issue, however, is immaterial for the purposes of preemption because Abbott put forward clear evidence that prior to October 2011 the FDA would have rejected any warning that the risk of autism increased from *in utero* exposure to Depakote, as the FDA specifically rejected such a warning in 2009 and again in February 2011. (Defs.' Ex. 22, ECF No. 88-22; Defs.' Ex. 16, ECF No. 88-16.)

Accordingly, Plaintiffs' claim that Defendants failed to warn of the risk of developmental delay is preempted. Plaintiffs' Motion for Partial Summary Judgment is thus **DENIED**.

b. Adequacy of Warning and Duty to Warn

After determining Plaintiffs' allegation that Defendants failed to warn of the risk of developmental delay, including autism, is preempted, the Court next turns to consider the parties' remaining arguments on the failure to warn claims. Plaintiffs claim that Abbott's 1996 Depakote label failed to warn that Depakote was more teratogenic than other similar drugs and that Depakote's teratogenic risks carried throughout pregnancy.

Drug manufacturers have a duty to warn of risks which they knew or reasonably should have known. O.R.C. § 2307.76(A). "[A] warning is 'adequate' . . . where, under all the circumstances, it reasonably discloses to the medical profession all risks inherent in the use of

the drug which the manufacturer knew or should have known to exist." *Seley v. G.D. Searle & Co.*, 67 Ohio St.2d 192, 198 (1981).

i. Sufficiency of Abbott's Warning of Depakote's Risk Beyond the First Trimester

In 1996, the "Usage in Pregnancy" section of Depakote's label read in pertinent part as follows:

> ACCORDING TO PUBLISHED AND UNPUBLISHED REPORTS, VALPROIC ACID MAY PRODUCE TERATOGENIC EFFECTS IN THE OFFSPRING OF HUMAN FEMALES RECEIEVING THE DRUG DURING PREGNANCY.
>
> . . . .
>
> THE INCIDENCE OF NEURAL TUBE DEFECTS IN THE FETUS MAY BE INCREASED IN MOTHERS RECEIVING VALPROATE DURING THE FIRST TRIMESTER OF PREGNANCY. THE CENTERS FOR DISEASE CONTROL (CDC) HAS ESTIMATED THE RISK OF VALPROIC ACID EXPOSED WOMEN HAVING CHILDREN WITH SPINA BIFIDA TO BE APPROXIMATELY 1 TO 2%.

(Ex. 4, 1996 Package Insert at PAGEID #: 13292 ECF 118-4.) In 2011, the Depakote label warns that "[t]he risk of major structural abnormalities is greatest during the first trimester; however, other serious developmental effects can occur with valproate use throughout pregnancy." (Pls.' Exhibit N at PAGEID #: 14486, ECF No. 127-17.) Plaintiffs acknowledge that "neural tube defects can only occur in the first trimester since the neural tube either closes normally or defects within roughly 28 days of conception." (Pls.' Mot.in Support of Dr. Piven's Testimony at 5, ECF No. 132.) Depakote's 1996 label warned of use "during pregnancy" throughout the label, only limiting the warning to the first trimester in regards to increased risk of spina bifida, a neural tube defect. (Ex. 4, 1996 Package Insert at PAGEID #: 13292 ECF 118-4.)

In support of their contention that Abbott's warning was insufficient in 1996, Plaintiffs argue, Abbot, "knowing that the brain continues to develop well past the first trimester, and knowing that Depakote had been associated with central nervous system deficiencies in children

exposed in-utero . . . should have known that Depakote's teratogenicity extended well past the first trimester and that such teratogenic effects manifested themselves in the developing fetal brain." (Pls.' Mot. in Support of Dr. Piven's Testimony at 5, ECF No. 132.) Abbott's label, however, did warn "valproic acid may produce teratogenic effect in the offspring of human females receiving the drug during pregnancy." (Ex. 4, 1996 Package Insert at PAGEID #: 13292 ECF 118-4.) Abbott's "during pregnancy" language included in its 1996 warning label is consistent with the language used in studies at the time. For example, the American College of Obstetricians and Gynecologists ("ACOG") educational bulletin on Seizure disorders in pregnancy dated December 1996 refers to the higher risk of birth defects in women treated with valproates "during pregnancy." (Defs.' Ex. 13, 1996 ACOG Bulletin at 4–5, ECF No. 88-13.) The only language limiting risk during pregnancy to the first trimester pertains to the risk of neural tube defects, which Plaintiffs acknowledge does not exist beyond the first trimester. (Pls.' Mot.in Support of Dr. Piven's Testimony at 5, ECF No. 132.)

Furthermore, the Court has already determined Plaintiffs' claim that Defendants failed to warn of the risk of developmental delay is preempted. Beyond the limitation already addressed, Plaintiffs' claim that Abbott failed to warn that Depakote use's risk continued during pregnancy beyond the first trimester is too intertwined with the developmental delay claim to remain. Plaintiffs point to Depakote's 2011 warning, which stated "[t]he risk of major structural abnormalities is greatest during the first trimester; however, other serious developmental effects can occur with valproate use throughout pregnancy," in support of their argument that the 1996 warning was insufficient. (Pls.' Exhibit N at PAGEID #: 14486, ECF No. 127-17.) The 2011 warning, however, would not have been allowed in 1996 as it relates the risk of "serious developmental effects" the FDA rejected on multiple occasions. As discussed above, in 2007, Abbott wrote the FDA proposing the inclusion of the language "[t]here have been reports of developmental delay in the offspring of women who have received valproate during pregnancy."

(Defs.' Ex. 20 at 3–4, ECF No. 88-20.) The FDA rejected the addition of that language. (*Id.*) Accordingly, even if Plaintiffs could show that a dispute in material fact remains that more than the "during pregnancy" language was necessary, to the extent the warning Plaintiffs seek references developmental delays, that claim is preempted.

ii. Sufficiency of Comparative Warning

Finally, Plaintiffs claim Abbott's warning was insufficient because of its "failure to warn that Depakote was more teratogenic than other similar drugs, and failure to warn of a statistically significant increased risk of malformations from use of Depakote compared to other similar drugs." (Pls.' Mot. in Opp. at 13, ECF No. 127.) Defendants argue that increased teratogenicity in Depakote as compared to similar drugs was unknown in 1996. (Defs.' Reply in Supp. at 11 n.5, ECF No. 161.) Plaintiffs do not offer evidence that in 1996 Abbott knew or should have known that Depakote was more teratogenic than other bipolar medications. Instead, Plaintiffs cite various expert reports, none of which state that in 1996 it was known Depakote was more teratogenic than other available bipolar medications.

Reviewing the evidence in the light most favorable for Plaintiff, other evidence in the record shows that in 1996, Plaintiff did not have other bipolar medication options that would have worked for her. Dr. Freeland, Plaintiffs' treating physician during her hospitalizations, testified that no other bipolar medications available in 1996 were viable options to treat Ms. Swanson. He stated "Other than lithium and carbamazepine, I currently can't think of another medication that was widely used of available specifically as a mood stabilizer." (Freeland Dep.91:17–25; 83:24; 84:1–4, ECF No. 89-3.) Dr. Freeland testified that he chose not to prescribe Carbamazepine because "Carbamazepine can be associated with side effects that I think potentially are more problematic than what typically might occur with Depakote. Those side effects could include, you know, a fairly severe rash, an effect on blood cell counts." (Freeland Dep. 84:24–25; 85:1–3.) Dr. Freeland had started Ms. Swanson on Lithium during her first hospitalization but ultimately switched her to Depakote because of adverse effects. (*See* Swanson Dep. at 114: 16–25, 115:1–23, 68: 6–21, ECF No. 99-7 ("And while I was in there the

second time is when I got my diagnosis as bipolar, and that's when they put me on the Depakote. They had put me, the first time, on Lithium and some other drugs. And I went home–when I was home that brief period, it was not good. I developed [Parkinson's]-like symptoms. And my dad had Parkinson's and that really scared me. So, you know, when I was home I freaked out. So, yeah, so Lithium did not work for me at all.")); (Freeland Dep. 84:1–4, ECF No. 89-3 ("My memory is that there were problems [from lithium] with persisting diarrhea that did not improve with reduction in dose, so it was decided to change medications.")

Accordingly, no dispute of material fact remains for the jury to decide.

B. Remaining Claims

Plaintiffs' remaining claims for breach of warranty, design defect, and negligent misrepresentation and fraud are all premised on Plaintiffs' claims that Abbott's warning was insufficient. As discussed in detail above, no genuine issue of material fact remains as to the adequacy of Depakote's label during the relevant time period. Accordingly, judgment is **GRANTED** for Defendants on Plaintiffs' remaining claims.

IV. CONCLUSION

Based on the foregoing, Defendants' Motion for Summary Judgment (ECF No. 88) is **GRANTED** and Plaintiffs' Motion for Summary Judgment (ECF No. 76) is **DENIED**. The pending *Daubert* motions are **DENIED as moot**. (ECF Nos. 74, 75, 84, 85, 86, 87.) The Clerk is directed to enter judgment in favor of the Defendants and close this matter.

IT IS SO ORDERED.

11-28-2017
DATE

EDMUND A. SARGUS, JR.
CHIEF UNITED STATES DISTRICT JUDGE